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over surface track regions of the substrate while producing cell traces, wherein the cell traces consist of material residues separated from the cells which contain genetic materials of the cells, and the genetic materials are subjected to amplification and the amplified genetic material is subjected to a genetic analysis.

REMARKS

Applicants submit this paper in response to the Office Action dated December 6, 2002 that was issued in the above-identified application. Applicants respectfully request reconsideration of the instant application in view of the amendments and remarks presented herein.

Applicants wish to thank the Examiner for taking the time to conduct an interview on January 29, 2003. During the interview, the prior art references cited by the Examiner were discussed and the Examiner suggested that addition of functional language to the pending claims might suffice for distinguishing the pending claims from the reference disclosures. In response, the newly added claims are directed to processes and compositions designed to identify at least one physical property of a test cell based on evaluating the composition of cell traces consisting of cell material separated from the test cell as it migrates over a surface track region. New claims 52-77 are fully supported by the application as filed and, therefore, do not constitute new matter.

Claims 1 and 27-51 which are pending have been canceled and replaced with new claims 52-77. The new claims appear in the preceding "IN THE CLAIMS" section. Attached hereto is a marked-up version of the changes made by the instant amendment captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE" and is included pursuant to 37

C.F.R. §1.121(c)(ii). Should any discrepancies be discovered, the version presented in the preceding "IN THE CLAIMS" section shall take precedence.

Claims are Novel Over the Cited Document

Claims 1, 27, 32, 42, and 50 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by French application FR 2743421 by Ronfard et al. (hereinafter "Ronfard"). The Examiner has alleged that Ronfard discloses a device with a substrate for adhesion of cell traces consisting of material residues separated from the cells.

Applicants traverse this rejection and assert that the instant claimed invention is not anticipated by Ronfard. Ronfard discloses a process that is designed to "evaluate the effect of various biological, chemical or physical conditions on the migrating capacity of the cells" (see, p.1, lines 2-4 of Ronfred). The process of Ronfred is based on measuring the migration of keratinocytes, wherein said keratinocytes merely serve as indicator cells for measuring migration. The process of Ronfard is not designed to identify any specific property of the keratinocyte, but rather, to determine whether a biological sample contains a molecule capable of affecting cell migration.

Applicants assert that Ronfard fails to disclose any process for identifying the biological properties of a test cell based on the analysis of cell traces consisting of cellular material separated from the test cells as they migrate over a substrate. In this regard, Applicants invite the Examiner's attention to the definition of "cell traces" provided in the instant application, *inter alia*, at page 7, lines 1-27. This description clearly indicates that "cell traces" according to the instant invention consist of cellular material derived from the cell being tested.

An important step in the process of the present invention is analysis of the cell traces to determine at least one biological property of the test cell. Ronfard simply fails to teach or suggest such analysis of cell traces to determine the biological properties of a test cell. Since Ronfard fails to teach each and every element of the claimed invention, Applicants respectfully request withdrawal of this rejection.

Claims are Nonobvious Over the Cited Documents

Claims 1 and 27, 29, and 30 have been rejected under 35 U.S.C. §103(a) as allegedly obvious over U.S. Patent No. 4,359,527 to Zetter (hereinafter "Zetter") in view of EP 0 347 210 by Loken et al. (hereinafter "Loken"). The Examiner has alleged that Zetter discloses a diagnostic assay wherein the area of a phagokinetic track left by at least one capillary endothelial cell is measured. The Examiner has acknowledged that Zetter does not disclose multiparameter analysis of cells in a body fluid. The Examiner has alleged that Loken discloses multiparameter analysis of cells in a body fluid.

Applicants traverse this rejection and assert that the instant claimed invention is not obvious over Zetter in view of Loken. Applicants respectfully point out that Zetter, like, Ronfard, **does not teach or suggest analysis of cell traces that consist of cellular material for identification of biological properties associated with a test cell.** Rather, Zetter discloses an assay for **detecting the presence in a test sample of a factor** associated with cancer cells. The method of Zetter relies on the measurement of phagokinetic tracts formed as **endothelial cells, which are merely indicator cells,** move across a substrate. See e.g. Col. 2, lines 2-4, and claim 1. Zetter describes phagokinetic tracts as follows: "The cells ingest the gold and, as they

move, leave bare areas or phagokinetic tracts as records of their movement." Col. 1, lines 38-40, emphasis added. Zetter *fails to teach or suggest cell traces that consist of cellular material* as required by Applicants'claims.

Although Loken discloses multiparameter analysis of cells in a body fluid, Loken fails to disclose an assay based on analysis of any kind of cell trace. Since Zetter and Loken, whether considered separately or in combination, fail to teach or suggest each element of the claimed invention, Applicants respectfully request withdrawal of this rejection.

Claims 1 and 38 have been rejected under 35 U.S.C. §103(a) as allegedly obvious over Zetter alone. The Examiner has alleged that Zetter discloses a diagnostic assay wherein the area of a *phagokinetic track* left by at least on capillary endothelial cell is measured. The Examiner has acknowledged that Zetter does not disclose predetermined surface tracts, but alleges that such would have been obvious to one of ordinary skill in the art.

Applicants traverse this rejection and assert that the instant claimed invention is not obvious over Zetter. Applicants respectfully point out that Zetter fails to teach or suggest each and element of independent claim 1, *i.e.* *analysis of cell traces consisting of cellular residues as a means for identifying a biological property of the test cell*, as discussed in the preceding paragraphs. Zetter merely describes a method for determining whether a biological sample contains a factor capable of modulating cell migration, a feature that has been shown to be associated with cancer cells. Applicants, therefore, respectfully request withdrawal of this rejection.

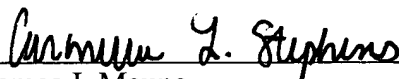
Claims 1 and 27, 32, 42-47, and 50 have been rejected under 35 U.S.C. §103(a) as allegedly obvious over Ronfard in view of the instant application. The Examiner has alleged that Ronfard discloses a diagnostic assay wherein cells adhere more poorly to the surface than on surface tract regions. The Examiner has acknowledged that Ronfard does not disclose the cell treatment and testing techniques of claims 43-47. The Examiner has alleged that Applicant's application indicates that such cell treatment and testing techniques are known in the relevant field of art.

Applicants traverse this rejection and assert that the instant claimed invention is not obvious over Ronfard. Applicants respectfully point out that the question of cell treatment and testing techniques recited in dependent claims 43-47 is moot in view of the failure of Ronfard to teach or suggest each and every element of independent claims 1, 42, and 50, *i.e.* cell traces consisting of cellular residue, as discussed in the preceding paragraphs. Applicants, therefore, respectfully request withdrawal of this rejection.

The Commissioner is hereby authorized to charge any fees due with this submission not otherwise enclosed herewith to Deposit Account No. 02-4377. Please credit any overpayment of fees associated with this filing to the above-identified deposit account. A duplicate of this page is enclosed.

Respectfully submitted,

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Enclosures

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Cancel claims 1 and 27-51.

Add the following new claims:

- 52. A process for cell traced based testing of biological cells wherein said testing identifies at least one property of said cells, wherein the cells to be tested are applied to a substrate, which is at least partially structured and/or surface modified, and move adhesively over the surface track regions of the substrate while producing cell traces, wherein the cell traces consist of material residues separated from the cells as the cells move over the surface track regions and wherein said cell traces are analysed to identify a property of said cells.
53. The process according to claim 52, wherein the amount, the geometry, the chemical composition, the passive electrical parameters, and/or the mechanical properties of the cell traces or of their components are detected for the cell testing.
54. The process according to claim 53, wherein filaments and membrane patches are detected to determine the quantity and geometry of the cell traces.
55. The process according to claim 53, wherein, to detect the composition of the cell traces, they are subjected to staining or marking for the performance of microanalytic processes.

56. The process according to claim 55, wherein the microanalytic processes comprise fluorescence measurements, measurements on the basis of isotope markings, or elemental analysis.
57. The process according to claim 53, wherein, to detect the composition of the cell traces, they are subjected to enzymatic decomposition.
58. The process according to claim 53, wherein the cell traces are tested with a high-resolution microscopy process.
59. The process according to claim 53, wherein cytoplasmic residues or genetic materials are detected in the cell traces.
60. The process according to claim 53, wherein the stability of the cell traces during mechanical, electrical, acoustic, optical, and/or chemical treatments is detected.
61. The process according to claim 53, wherein, to determine the passive electrical parameters of the cell traces, their impedance, breakthrough resistance, non-linear behaviour, and/or heating during current flow are detected.
62. The process according to claim 53, wherein, to determine mechanical properties of the cell traces, their elasticity or plasticity is detected.
63. The process according to claim 52, wherein a duplication of components of the cell traces is performed to produce reference material.

64. The process according to claim 52, wherein the cell traces are produced in predetermined surface track regions, which are at least partially microstructured and/or modified for amplified adhesion of the cells.
65. The process according to claim 52, wherein the cells are subjected, after the production of the cell traces, to a medical or measurement technology application, cryopreservation, or further cultivation.
66. The process according to claim 52, wherein multiple cell traces are produced and tested on multiple parallel tracks.
67. The process according to claim 52, wherein cell traces are produced on intersecting tracks and the mutual interactions of the participating cells and/or cell traces are tested at intersection regions of the intersecting tracks.
68. A device for cell trace based testing of biological cells comprising a substrate having surface regions and surface track regions, wherein said cells adhere more poorly on the surface regions than on surface track regions, and wherein the surface track regions are arranged for the adhesion of cell traces consisting of material residues separated from the cells.
69. The device according to claim 68, wherein the substrate is structurally and/or chemically modified in the surface regions and/or the surface track regions, in order to suppress and/or encourage the adhesion of cell traces.

70. The device according to claim 68, wherein the substrate is part of a microsystem on which the surface regions and the surface track regions are implemented, with the surface track regions forming at least one straight track.
71. The device according to claim 68, wherein the substrate consists of glass, silicon, or a plastic.
72. The device according to claim 68, wherein multiple surface track regions in the form of a group of parallel tracks or intersecting tracks are formed.
73. The device according to claim 68, wherein the substrate is in two parts, with the surface track regions located on one of the substrate parts.
74. A process for cell trace based cultivation of biological cells, in which the cells are applied to an at least partially structured and/or surface modified substrate and move adhesively over the surface of the substrate while producing cell traces, wherein the cell traces consist of material residues separated from the cells, and cultivation of the same or a different type of cells is performed on the cell traces.
75. The process according to claim 74, wherein the biological cells are tissue producing cells and the substrate comprises an implant material.
76. A process of testing of the properties of cells for medical, biochemical, and/or pharmacological purposes, or for biocompatible modification of the surfaces of implant materials, by using material residues, which are formed by biological cells as cell traces on substrates.

77. A process for the manipulation of biological cells, in which the cells are applied to a substrate, which is at least partially structured and/or surface modified, and move adhesively over surface track regions of the substrate while producing cell traces, wherein the cell traces consist of material residues separated from the cells which contain genetic materials of the cells, and the genetic materials are subjected to amplification and the amplified genetic material is subjected to a genetic analysis.